

REMARKS

After amendment, claims 37-68 are presently pending in the present application. Claims 1-36 and 40-41 were previously cancelled, claim 37 previously amended and claims 42-66 were previously added. The amendment to claim 42 presented herein is supported by the originally filed application and claims. Claim 42 has been amended and new claims 67-68 have been added to address the Examiner's concerns regarding the elected invention. *In toto*, the claims have been drafted to reflect the Examiner's view of enablement of specific mutations which have been presented in the application and to address the election issue. The specific mutations have been incorporated into the claims. No new matter has been added by way of this amendment. It is respectfully submitted that amended claim 42, new claims 67 and 68 and claims 37-68 now address the Examiner's concerns.

The Examiner had variously objected to or rejected the originally filed claims of the instant application under 35 U.S.C. §112, first and second paragraphs and §102 for the reasons stated in the August 8, 2006 office action. Applicants have previously addressed each of the Examiner's objections/rejections in the response submitted November 13, 2006. Applicants shall address the enablement issue with respect to the amendment of claim 42 and newly submitted claims 67-68 herein, inasmuch as each of the other objections/rejections previously raised were addressed in the November 13, 2006 office action. Our response to those objections/rejections, where relevant, are referenced here.

The 35 USC § 112, First Paragraph Rejection

The Examiner previously had rejected the originally filed claims under 35 U.S.C. §112, first paragraph, as being non-enabled for the reasons which were set forth in the August 2006 office action on pages 5-10. The Examiner had indicated that certain mutants were enabled. Applicants previously amended the claims to reflect the Examiner's indication of enabled subject

matter. In the present response, the claims have been amended to maintain compliance with 35 U.S.C. §112, first paragraph and to address the Examiner's concerns regarding the elected invention as set forth in the March 27, 2007 office action.

The comments made in the November 13, 2006 response to the outstanding office action regarding enablement are referenced here. The previously filed claims were enabled for the reasons stated in that November, 2006 paper.

With respect to the enablement of the K180A mutation (SEQ ID No 10), we offer the following comments. The examiner states "Furthermore, according to the specification at p. 23, the SEQ ID NO: 10 mutant IGFBP-2 molecule is *not* resistant to proteolysis, making it even more unpredictable as to whether or not this mutant would be capable of increased binding of IGF upon contact with an extracellular matrix or exposure to a protease"

Applicant points out that this is incorrect, there is no data that teaches against enablement of K180A. There is, in fact, no data directly on this issue with respect to K180A. It is pointed out that, to date, the single mutants K180A and K181A have not been tested individually.

The Examiner points out that "While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited."

Applicant submits that with respect to K180A and K181A this is at an extreme end of the spectrum of predictability, for two reasons. Firstly, an alteration of both residues leads to the effect. Secondly there is a remote possibility that only one of the amino acid alterations leads the change, but it is submitted to be highly unlikely. The two residues are in adjacent position (180, 181), both are identical, being lysine residue and as such have identical characteristics, and are both changed to an identical new residue (namely alanine). This near identity of position and identity

of nature of the amino acids means that there is a very high likelihood that they would co-contribute to the effect. Accordingly, *prima facie* it is submitted it would be an expectation that modification of both of these residues individually will have an effect, not necessarily an identical effect, but a co-contributing effect. The nearly identical positioning of the residues and their identical nature gives a high expectation of that. It is submitted that it is predictable to individually alterations at position 180 and 181 are co-contributors to the effect and that individual residue alterations will also have an effect if not as pronounced.

It is respectfully submitted that the presently claimed invention complies with the requirements of 35 U.S.C. §112, first paragraph. Favorable consideration of this application is respectfully solicited.

For all of the above reasons, it is respectfully submitted that the present application is now in condition for allowance and such action is earnestly solicited. 38 claims (including 1 independent claim) have been cancelled previously cancelled, 25 claims (including 2 independent claims for a total of three independent claims pending in the present application) were previously added and two additional claims were added to the present application. Three independent claims remain pending in the present application. No fee is therefore due for the presentation of this amendment.

The Commissioner is authorized to charge any fee or credit any overpayment to deposit account 04-0838.

Respectfully submitted,
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I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to:
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Henry D. Coleman